

**Remarks/Arguments**

Claims 42-46 and 49-51 are pending and remain rejected in this application. The rejections to the claims are respectfully traversed.

**Request for consideration of change of address (second time)**

A Revocation of Power of Attorney and change of address was mailed to the USPTO in this case on February 20, 2003. A stamped, return postcard was received from the USPTO dated February 27, 2003. Applicants respectfully request that the Examiner note the address change and kindly direct all correspondence pertaining to this case to:

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**Claim Rejections – 35 USC § 101 and 112, First Paragraph**

Claims 42-46 and 49-51 remain rejected under 35 U.S.C. §101 allegedly because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility.

Claims 42-46 and 49-51 remain rejected under 35 U.S.C. §112, first paragraph, allegedly since the claimed invention is not supported by either a clear asserted utility or a well established utility, one in the art clearly would not know how to use the claimed invention.

The Examiner states that "(t)he only point of disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility." The Examiner does not find the Declaration by Dr. Fong persuasive. While the Examiner agrees that "(t)here appears to be no disagreement on the role of proinflammatory molecules as presented in the Declaration of Fong and the view existing in the art," the Examiner argues that "...proinflammatory proteins.... are known to play a key role in the migration of inflammatory cells in autoimmune diseases and in invasive cancers," "it is also recognized in the art that the spectrum of action of proinflammatory molecules is very broad and also dependent on the timing and level of production of a specific proinflammatory protein." Based on the review article by Falcone *et al.*, the Examiner points out that "the art acknowledges the broad range and complexity of functions of proinflammatory

proteins and, therefore, the specific function of a particular molecule cannot be predicted based solely on the notion that it belongs to a family of proinflammatory proteins." (Emphasis added). From these statements, it seems that, while the Examiner acknowledges that a proinflammatory molecule may play a role in diseases such as, for example, in autoimmune diseases, invasive cancers, etc., the 'specific function' of a particular proinflammatory molecule cannot be predicted based solely on the notion that it belongs to a family of proinflammatory proteins. Applicants respectfully submit that the Examiner's position on "utility requirements" for a molecule is legally incorrect, and respectfully traverse this rejection.

#### Utility – Legal Standard

The well established case law is clearly reflected in the Utility Examination Guidelines ("Utility Guidelines"),<sup>1</sup> which acknowledge that an invention complies with the utility requirement of 35 U.S.C. §101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility." The case law has also clearly established that applicants' statements of utility are usually sufficient, unless such statement of utility is unbelievable on its face.<sup>2</sup> The PTO has the initial burden that applicants' claims of usefulness are not believable on their face.<sup>3</sup> In general, an Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope."<sup>4,5</sup> The Utility Guidelines also restate the Patent Office's long established position that:

"by statute, a patent is required to disclose one practical utility. If a well-established utility is readily apparent, the disclosure is deemed to be implicit."

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<sup>1</sup> 66 Fed. Reg. 1092 (2001).

<sup>2</sup> *In re Gazave*, 379 F.2d 973, 154 U.S.P.Q. (BNA) 92 (C.C.P.A. 1967).

<sup>3</sup> *Ibid.*

<sup>4</sup> *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. (BNA) 288, 297 (CCPA 1974).

<sup>5</sup> See, also *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *In re Irons*, 340 F.2d 974, 144 USPQ 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (CCPA 1977).

The Utility Guidelines further state that:

"the record of any issued patent typically reflects consideration of a number of references in the prior art that the applicant or the Examiner considered material to the claimed invention. These references often indicate uses for related inventions, and any patents listed typically disclose utilities or related inventions. Thus, even when the Examiner does not identify a well-established utility, the record as a whole will likely disclose readily apparent utilities.....a well-established utility is a specific, substantial and credible utility that must be readily apparent to one skilled in the art." (Emphasis added).

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a particular composition of matter is useful as a diagnostic tool, without also identifying the conditions that are to be diagnosed using the diagnostic tool. However, when the condition that is capable of being diagnosed is specifically identified and linked to the claimed subject matter, the asserted utility satisfies the "specificity requirement.

Later, in *Nelson v. Bowler*<sup>6</sup> the CCPA acknowledged that tests evidencing pharmacological activity of a compound may establish practical utility, even though they may not establish a "specific" therapeutic use. The court held that "since it is crucial to provide researchers with an incentive to disclose pharmaceutical activities in as many compounds as possible, we conclude adequate proof of any such activity constitutes a showing of practical utility."<sup>7</sup> (Emphasis added).

In *Cross v. Iizuka*<sup>8</sup> the CAFC reaffirmed *Nelson*, and added that *in vitro* results might be sufficient to support practical utility, explaining that "*in vitro* testing, in general, is relatively less complex, less time consuming, and less expensive than *in vivo* testing (emphasis added). Moreover, *in vitro* results with the particular pharmacological activity are generally predictive of

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<sup>6</sup> *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (C.C.P.A. 1980).

<sup>7</sup> *Id.* at 856, 206 U.S.P.Q. (BNA) at 883.

<sup>8</sup> *Cross v. Iizuka*, 753 F.2d 1047, 224 U.S.P.Q. (BNA) 739 (Fed. Cir. 1985).

*in vivo* test results, i.e. there is a reasonable correlation there between.<sup>9</sup> The court perceived "No insurmountable difficulty" in finding that, under appropriate circumstances, "in vitro testing, may establish a practical utility."<sup>10</sup>

In interpreting the "substantial utility" requirement, in *Brenner v. Manson*<sup>11</sup> the Supreme Court held that the quid pro quo contemplated by the U.S. Constitution between the public interest and the interest of the inventors required that a patent applicant disclose a "substantial utility" for his or her invention, i.e. a utility "where specific benefit exists in currently available form."<sup>12</sup> The Court concluded that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. A patent system must be related to the world of commerce rather than the realm of philosophy."<sup>13</sup>

In explaining the "substantial utility" standard, M.P.E.P. §2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "'substantial' utility"<sup>14</sup> (emphasis added). Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement,<sup>15</sup> gives the following instruction to patent examiners:

"If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

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<sup>9</sup> *Id.* at 1050, 224 U.S.P.Q. (BNA) at 747.

<sup>10</sup> *Id.*

<sup>11</sup> *Brenner v. Manson*, 383 U.S. 519, 148 U.S.P.Q. (BNA) 689 (1966).

<sup>12</sup> *Id.* at 534, 148 U.S.P.Q. (BNA) at 695.

<sup>13</sup> *Id.* at 536, 148 U.S.P.Q. (BNA) at 696.

<sup>14</sup> M.P.E.P. §2107.01.

<sup>15</sup> M.P.E.P. §2107 II(B)(1).

Moreover, the Utility Guidelines make clear that the requirement for the asserted utility be "substantial" arises solely for the purpose of excluding:

"'throw-away' or 'insubstantial'.....utilities, such as the use of a complex invention as landfill, as a way of satisfying the utility requirement of 35 U.S.C. §101."<sup>16</sup> (emphasis added).

#### **Proper Application of the Legal Standard**

The data presented in the present application, upon which applicants rely for utility and is currently disputed, is presented in Example 77 (page 210, lines 22- "skin vascular permeability assay"), which is a well-described, dye-based assay routinely employed to identify proinflammatory molecules that cause the influx or infiltration of proinflammatory cells into a site of vascular leakage (or edema). In other words, a positive hit for PRO266 in the proinflammatory assay allows one skilled in the art to use PRO266 as a therapeutic target, since using PRO266 "to recruit proinflammatory cells into say, a tumor site" is useful to prevent tumor invasiveness, and/or possibly, to destroy tumor cells. Alternatively, blocking its function would be useful to 'decrease' inflammation, for instance, in autoimmune diseases. Therefore, the skilled artisan would readily recognize a utility for the PRO266 polypeptide based on its positive hit in the proinflammatory skin vascular permeability assay.

Contrary to the Applicants assertion of utility herein, however, the Examiner alleges that the positive hit in the skin vascular permeability assay does not render the presently claimed polypeptides patentably useful. Applicants respectfully submit, however, that upon application of the appropriate legal standards described above, the proper conclusion is that the present application does, in fact, disclose a patentable utility for the claimed invention.

##### **(i) The Requirement for a "specific" utility**

As described above, Applicants have clearly demonstrated that PRO266 is detectably a proinflammatory molecule based on the skin vascular permeability assay. In the non-final Office action of January 3, 2005, the Examiner asserts:

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<sup>16</sup> 66 Fed. Reg. 1092, 1098 (2001).

"the 'specific function' of a particular proinflammatory molecule cannot be predicted based solely on the notion that it belongs to a family of proinflammatory proteins." (Emphasis added).

Applicants respectfully submit that a 'specific function' to be disclosed for patentable molecule is not a requirement for "specificity" under 35 U.S.C. § 101. Even if a proinflammatory protein may have a "broad range and complexity of functions" and "a specific function of a particular proinflammatory molecule cannot be predicted, prediction of specific function is not a utility requirement. As described above, the "specificity" requirement under 35 U.S.C. § 101 merely requires a patent applicant to set forth and describe the asserted utility with specificity. Applicants have asserted that the claimed invention is specifically useful as "a therapeutic target" at least to prevent tumor invasiveness, and/or possibly, to destroy tumor cells or alternatively, antagonistic antibodies to PRO266 are useful to 'decrease' inflammation, for instance, in autoimmune diseases. Applicants have specifically identified and described diseases for which the invention is therapeutically useful. Therefore, applicants respectfully submit that this clearly satisfies the "specificity requirement".

**(ii) The Requirement for a "substantial" utility**

As described above, as set forth in the Utility Guidelines, for a claimed invention to be "substantial," the claimed invention must serve a "practical purpose" which is not a "throw-away or insubstantial [use], such as the use of a complex invention as a landfill (Emphasis supplied).

In this regard, the Examiner states:

"It is a matter of law that the claimed invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. In the instant case, significant further research would have to be conducted to identify diseases, which could be treated by administration of antibodies to PRO266 proteins."

Applicants strongly disagree. In essence, the Examiner's argument is that being able to identify PRO266 as a therapeutic proinflammatory target is (i) "impractical", (ii) a "throw-away" use which is akin to the use of "a complex invention as a landfill", and is (iii) "insubstantial". Applicants respectfully submit that is there is nothing farther from the truth. Scientific and

medical researchers spend millions of dollars each year to develop new, and useful proinflammatory therapeutic targets which are useful for treating invasive cancers or antagonistic antibodies that are useful against autoimmune diseases. The discovery of PRO266 as a proinflammatory molecule provides for the first time the ability to exploit this target as a therapeutic agent for treating the above mentioned diseases. This does not mean that the invention is not useful in its currently available form. As such, Applicants reiterate the M.P.E.P. §2107.01 which cautions, however, that

"Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility"(emphasis added).

Applicants submit that the utility presently asserted for the claimed invention meets the "substantial" requirement set for by the Utility Guidelines and required by the U.S. Supreme Court in *Brenner v. Manson*, 383 U.S. 519 (1966).

Further, as discussed above, PRO266 is useful at least as a therapeutic target to prepare anti-inflammatory agents or as an agent that recruits the inflammatory process for treatment in conditions like invasive cancer, etc. Therefore, one skilled in the art would not know how to make and use the claimed polypeptides based on the instant disclosure and the advanced knowledge of the skilled artisan in the art.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present utility rejection and the rejection under 35 U.S.C. §112, first paragraph.

#### **Claim Rejections – 35 U.S.C. § 112, first paragraph**

Claims 42-43 remain rejected under 35 U.S.C. §112, first paragraph, allegedly as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had "possession" of the claimed invention.

### **Written description standard**

Whether a specification shows that Appellants were in possession of the invention as of the effective filing date of an application is a factual determination, reached by the consideration of a number of factors, including level of knowledge and skill in the art, and teaching provided by the specification. The inventor is not required to describe every single detail of his invention. An Applicant's disclosure obligation varies according to the art to which the invention pertains.

### **Arguments**

The present invention is from the field of recombinant DNA technology. In particular, the invention defined by the claims rejected concerns isolated polypeptides having 95%, or 99% sequence identity with identity to a particular polypeptide sequence, SEQ ID NO: 91, that has been reduced to practice, further, which induces an inflammatory response. It is well established that the level of skill in this field is relatively high, and is represented by a Ph.D. scientist having several years of experience in the pertinent field. Accordingly, the teaching imparted in the specification must be evaluated through the eyes of a highly skilled artisan as of the date the invention was made.

The written description requirements are well-explained in Example 14 of the Written Description guidelines issued by the U.S. Patent Office. The instant specification evidences actual reduction to practice of full-length native human PRO266 polypeptide (SEQ ID NO: 91), with or without its signal sequence. In addition, the specification provides detailed description about the cloning and expression of variants of the polypeptide PRO266 (see, e.g. pages 154-155 and 196-201), and describes an assay for testing the ability of a PRO266 polypeptide, including variants of the native sequence, to induce a proinflammatory response. Thus, Applicants indicate that the genus of proteins that are variants of PRO266 must also possess the an ability to induce a proinflammatory response and must have at least 95% identity to the sequence of SEQ ID NO: 91. In view of this disclosure of the proinflammatory assay which is useful for identifying the variants with at least 95% identity SEQ ID NO: 91, a person skilled in the art would recognize that Applicants were in possession of the members of the genus which have the necessary common attributes as described at the effective filing date of the present application.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

**Claim Rejections – 35 U.S.C. § 112, Second Paragraph**

Claims 42-46 and 49-51 are rejected under 35 U.S.C. §112, second paragraph for being indefinite in reciting "; or" in section (c) of the claims. Claims 45-46 and 49-51 are indefinite for being dependent from indefinite claims.

Applicants have deleted references to "; or" in pending claims 42-44. Therefore, dependent claims 45-46 and 49-51 should also be definite. Accordingly, this rejection should be withdrawn.

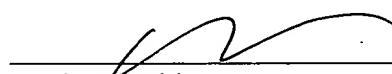
The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

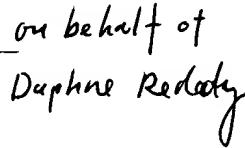
Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C29). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

(43,626)

Date: July 7, 2005

  
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